General

Guideline Title

Bipolar disorder.

Bibliographic Source(s)

Singapore Ministry of Health. Bipolar disorder. Singapore: Singapore Ministry of Health; 2011 Nov. 68 p. [125 references]

Guideline Status

This is the current release of the guideline.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- May 10, 2016 – Olanzapine: The U.S. Food and Drug Administration (FDA) is warning that the antipsychotic medicine olanzapine can cause a rare but serious skin reaction that can progress to affect other parts of the body. FDA is adding a new warning to the drug labels for all olanzapine-containing products that describes this severe condition known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).
- May 3, 2016 – Aripiprazole (Abilify, Abilify Maintena, Aristada): The U.S. Food and Drug Administration (FDA) is warning that compulsive or uncontrollable urges to gamble, binge eat, shop, and have sex have been reported with the use of the antipsychotic drug aripiprazole (Abilify, Abilify Maintena, Aristada, and generics). These uncontrollable urges were reported to have stopped when the medicine was discontinued or the dose was reduced. These impulse-control problems are rare, but they may result in harm to the patient and others if not recognized.

Recommendations

Major Recommendations

Definitions of the level of evidence (1++, 1+, 1-, 2++, 2+, 2-, 3, 4) and the grades of recommendations (A, B, C, D, GPP) are defined at the end of the "Major Recommendations" field.

Definitions and Diagnosis

GPP - When diagnosing bipolar disorder, a careful clinical assessment that includes a longitudinal history, as well as obtaining a history of mania and hypomania in patients with a first presentation of depression, should be performed. (GPP)

C - The use of screening instruments in day-to-day practice in primary and tertiary settings is not recommended. (Grade C, Level 2+)

Acute Treatment

A - Haloperidol may be used for the treatment of acute mania. (Grade A, Level 1+)

A - Aripiprazole, olanzapine, quetiapine, risperidone, or ziprasidone may be used for the treatment of acute mania. (Grade A, Level 1+)

A - Combination pharmacotherapy with an antipsychotic and a mood stabiliser may be used for patients showing inadequate response to mood stabiliser monotherapy. (Grade A, Level 1+)

A - Lithium monotherapy may be used for the treatment of acute mania. (Grade A, Level 1+)

A - Sodium valproate monotherapy may be used for the treatment of acute mania. (Grade A, Level 1+)

A - Carbamazepine monotherapy may be used for the treatment of acute mania. (Grade A, Level 1+)

A - Lamotrigine should not be used for the treatment of acute mania as it lacks efficacy in this area. (Grade A, Level 1+)

A - Clonazepam or lorazepam (intramuscular [IM] or oral) may be used in the acute treatment of agitation in mania. (Grade A, Level 1+)

A - Haloperidol (IM or oral), olanzapine (IM or oral), quetiapine (oral) or aripiprazole (IM) may be used in the acute treatment of agitation in mania. (Grade A, Level 1+)

A - If antidepressants are to be used in combination with mood stabilisers as first-line treatment for the acute treatment of bipolar depression, they should be used cautiously due to conflicting evidence of efficacy. (Grade A, Level 1+)

GPP - The lowest therapeutic dosage of antidepressants, for the shortest required period of time, should be used for patients who continue to be depressed despite the optimal use of mood stabilisers. (GPP)

A - Quetiapine monotherapy, olanzapine monotherapy or olanzapine-fluoxetine combination may be used in the treatment of bipolar depression. (Grade A, Level 1+)

A - Monotherapy with sodium valproate or carbamazepine is not recommended in the treatment of bipolar depression due to conflicting evidence regarding efficacy. (Grade A, Level 1+)

A - There is insufficient evidence to recommend lamotrigine monotherapy in the treatment of bipolar depression. However, it is recommended as an add-on for patients already on lithium for treatment of bipolar depression. (Grade A, Level 1+)

A - Lithium may be used in the treatment of bipolar depression. (Grade A, Level 1+)

A - Consider using sodium valproate or quetiapine as first-line treatment in patients with rapid cycling. This may be combined with lithium. (Grade A, Level 1+)

A - A combination of lithium and lamotrigine may be considered as an alternative treatment for rapid cycling. (Grade A, Level 1+)

GPP - Non-pharmacological treatments should not be used for patients with rapid cycling bipolar disorder due to insufficient evidence. (GPP)

A - Mood stabilisers may be used when treating mixed states. Of these, valproate and carbamazepine should be preferred over lithium as there is more evidence for the efficacy of valproate and carbamazepine than for lithium. (Grade A, Level 1+)

B - Electroconvulsive therapy can be considered for manic and depressive episodes which are severe or which fail to respond to pharmacological interventions, or when pharmacological interventions are not possible. (Grade B, Level 2++)

C - Consider the use of electroconvulsive therapy as anti-manic and antidepressive treatment in mixed states that are severe or fail to respond to pharmacological interventions, or when pharmacological interventions are not possible. (Grade C, Level 2+)

Maintenance

A - Lamotrigine can be used for prophylaxis in patients who have initially stabilised with lamotrigine. (Grade A, Level 1+)

A - Lithium, valproate, or olanzapine may be used as maintenance therapy in preventing relapse to either pole of illness in patients with bipolar disorder. (Grade A, Level 1+)

A - Aripiprazole may be used as maintenance therapy in bipolar patients with recent manic or mixed episode. (Grade A, Level 1+)

A - Quetiapine, in combination with lithium or valproate, may be used as maintenance therapy in patients with bipolar I disorder. (Grade A, Level 1+)

A - To minimize the risk of manic switching and/or rapid cycling, patients whose depressive symptoms have remitted for at least 8 weeks from an acute depressive episode may have their antidepressant medication gradually discontinued over several weeks, whilst maintaining them on their mood stabiliser medication. (Grade A, Level 1+)

A - Patients should not be routinely continued on their antidepressant treatment for long-term as they offer minimal to no significant continuing benefits or effects on depressive episode prevention or enhanced remission rates. (Grade A, Level 1+)

A - Maintenance medications for bipolar disorder should not be discontinued, in view of the high risk of relapse. (Grade A, Level 1+)

A - If discontinuation of maintenance medications is planned, it should be performed by gradual tapering of the dosage over several weeks. (Grade A, Level 1+)

A - Lithium and valproate may be used as maintenance therapy for patients with rapid cycling bipolar disorder. (Grade A, Level 1+)

B - Patients with rapid cycling bipolar disorder should not be routinely continued on antidepressant therapy after achieving remission as it does not offer significant clinical benefit in preventing relapse. (Grade B, Level 2++)

Psychological Interventions

GPP - Whenever possible, health professionals should provide psychoeducation to patients with bipolar disorder, and their families/caregivers. (GPP)

A - Upon identification of early warning signs/relapse signatures by individuals or family members/caregivers, individuals can use the plan of action that they developed based on these early warning signs. This plan of action should be a collaborative effort between the patient, family members/caregivers and healthcare professionals. (Grade A, Level 1+)

A - Cognitive behavioural therapy, family therapy or interpersonal social rhythms therapy may be considered as part of the treatment plan for bipolar depression. (Grade A, Level 1+)

Reproductive Health Issues

A - Women on combined oral contraceptive pills who are concurrently taking carbamazepine and/or lamotrigine should be advised of the risk of decreased contraceptive effect as a result of drug interactions. (Grade A, Level 1+)

B - Use of sodium valproate in women of childbearing age should be balanced against the risk of decreased fertility, foetal malformations and perinatal complications. (Grade B, Level 1+)

A - Periconceptional folate supplementation should be prescribed to protect against neural tube defects. (Grade A, Level 1+)

D - Abrupt discontinuation (i.e., less than 2 weeks) of mood stabilisers should be avoided if possible, in order to lessen the chance of relapse. (Grade D, Level 3)

GPP - Consider switching to antipsychotic treatment, or gradual decrement (over 15–30 days) of monotherapy mood stabiliser to the lowest effective amount in divided doses during pregnancy; concurrent careful foetal monitoring is recommended. (GPP)

GPP - Consider resuming mood stabiliser treatment immediately postpartum as this is a period of vulnerability to relapse. (GPP)

B&GPP - Sodium valproate and carbamazepine are preferable to lithium and lamotrigine during breastfeeding (Grade B, Level 2++); mothers who require the latter two medications may be advised to consider abstinence from breastfeeding for the infant's safety. (GPP)

GPP - In the event of breastfeeding while taking mood stabilisers, consider administering feeds before taking medication and discarding the first post-dose batch of expressed milk, so as to minimise the infant's consumption of medication via breast milk. (GPP)

B - First-trimester paroxetine use should be avoided as it is associated with increased risk of serious congenital (particularly cardiac) defects. (Grade B, Level 2++)

B - Selective serotonin reuptake inhibitors should be used judiciously in late pregnancy because of associations with persistent pulmonary hypertension of the newborn and neonatal behavioural syndrome. (Grade B, Level 2++)

GPP - While there is no evidence for routine monitoring for congenital malformations during antenatal use of antidepressants, careful foetal monitoring is recommended nonetheless. (GPP)

D - Women who are planning conception should be advised that antipsychotics are associated with hyperprolactinemia and amenorrhea, which may affect fertility (and predispose toward premature bone loss). (Grade D, Level 3)

D - Typical antipsychotics, such as chlorpromazine and haloperidol, may be considered for treatment of pregnant women with bipolar disorder, as they appear less likely than atypical antipsychotics to cause metabolic complications and other serious adverse effects. (Grade D, Level 3)

GPP - When considering antipsychotics for pregnant women, the clinical presentation and side effect profile should also be considered. For instance, previous poor response or side effects to typical antipsychotics should merit consideration of an atypical antipsychotic. (GPP)

GPP - Weight, blood sugar and blood pressure should be monitored in pregnant women on atypical antipsychotics. (GPP)

GPP - When antipsychotics are used in pregnant women, close and careful foetal monitoring via regular visits and scans is recommended. (GPP)

GPP - In the event of breastfeeding while taking antipsychotics, consider administering feeds before taking medication and discarding the first post-dose batch of expressed milk to minimise the infant's consumption of medication via breast milk. (GPP)

C - Benzodiazepines should be avoided in pregnancy. (Grade C, Level 2+)

D - Electroconvulsive therapy may be considered as a treatment option in pregnancy for the same indications as in nonpregnant patients. (Grade D, Level 3)

Substance Misuse

A - Addiction disorders in patients with bipolar disorder should be treated. (Grade A, Level 1+)

GPP - Patients with dual diagnosis of bipolar disorder and addiction disorders should be treated in an integrated specialist treatment centre. (GPP)

Suicide Prevention

C - Clinicians should routinely assess risk of suicide in all patients with bipolar disorder. (Grade C, Level 2+)

Monitoring

B - During each review, clinical assessment of cardiovascular risk factors (e.g., obesity, smoking) should be performed for all patients with bipolar disorders. (Grade B, Level 2++)

GPP - Prior to starting treatment, doctors should obtain a patient's personal and family history of obesity, diabetes, dyslipidaemia, hypertension and cardiovascular disease. (GPP)

GPP - A patient's alcohol and smoking history, height, weight (including the calculation of body mass index) and blood pressure measurements, together with fasting blood (plasma) glucose level and lipid profile assessment should be obtained at baseline. This clinical monitoring should also be repeated at regular planned intervals. (GPP)

GPP - Consider using the Clinical Global Impression scales (both severity and improvement component scales) to measure illness severity and treatment progress during consultations. (GPP)

Definitions:

Levels of Evidence

Level	Type of Evidence
1++	High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

Level	Type of Evidence
1++	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g., case reports, case series
4	Expert opinion

Grades of Recommendation

Grade	Recommendation
A	At least one meta-analysis, systematic review of randomised controlled trials (RCTs), or RCT rated as 1++ and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+
GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Bipolar disorder

Guideline Category

Diagnosis

Evaluation

Management

Risk Assessment

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Obstetrics and Gynecology

Psychiatry

Psychology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Guideline Objective(s)

To provide a framework to diagnose and initiate treatment for adult patients with bipolar disorder and continue maintenance treatment

Target Population

Adult patients with bipolar disorder

Interventions and Practices Considered

Diagnosis/Evaluation/Risk Assessment

1. Clinical assessment including longitudinal history, history of mania and hypomania
2. Alcohol and smoking history, height, weight (including the calculation of body mass index) and blood pressure measurements, together with fasting blood (plasma) glucose level and lipid profile assessment
3. Clinical Global Impression (CGI) scales (both severity and improvement component scales)
4. Routine use of screening instruments in primary and tertiary settings (not recommended)
5. Routine assessment for risk of suicide

Management/Treatment

1. Pharmacotherapy
    - Antipsychotics (e.g., haloperidol)
    - Atypical antipsychotics (e.g., aripiprazole, olanzapine, quetiapine, risperidone, ziprasidone)
    - Lithium
    - Antiepileptics (e.g., sodium valproate, carbamazepine, lamotrigine)
    - Selective serotonin reuptake inhibitors (e.g., fluoxetine)
    - Benzodiazepines (e.g., clonazepam or lorazepam)

    - Combination pharmacotherapy (as indicated)
2. Gradual medication tapering to discontinuance
3. Electroconvulsive therapy
4. Psychological interventions
    - Psychoeducation
    - Identification of early warning signs/relapse signatures and development of plan of action
    - Cognitive behavioural therapy, family therapy or interpersonal social rhythms therapy
5. Management of acute episodes
6. Maintenance treatment
7. Management of reproductive health issues for women
8. Management of addiction disorders in bipolar patients (referral to integrated specialist treatment center)
9. Ongoing monitoring (CGI scales, cardiovascular risk factors)

Major Outcomes Considered

- Signs and symptoms of bipolar disorders and mania including anxiety, insomnia, agitation, seizures, muscle spasms and alcohol withdrawal
- Side effects of medications

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Searches were run on PubMed (1966-2011); EMBASE (1947-2011), the Cumulative Index to Nursing & Allied Health (CINAHL) database (1984-2011) and PsycINFO (1806-2011) for searching evidence related to bipolar disorder. Additionally both the Cochrane Library (2011, Issue 3) and Centre for Reviews and Dissemination databases (DARE, NHS EED and HTA) were searched for systematic reviews and cost effectiveness studies. The guideline developers also performed Internet search on websites of guidelines agencies and professional societies that published clinical practice guidelines and consensus evidence on the given condition. These include the search for the last five years of the existing clinical practice guidelines (2006-2010) from sources of overseas guidelines agencies and professional bodies, e.g., National Guideline Clearinghouse, National Health Service (NHS) National Library of Guidelines, the Guidelines International Network, Agency for Healthcare Research and Quality (AHRQ), Canadian Medical Association (CMA) Clinical Practice Guidelines, New Zealand Guidelines Group, Australia's Clinical Practice Guidelines Portal websites.

Inclusion/exclusion criteria were used specific to the clinical questions to be answered. In general, search filters were used to further focus the type of studies to randomised controlled trials and systematic reviews of randomised controlled trials. If there is a paucity of higher level evidence, lower level evidence may be considered.

All searches used keywords and MeSH headings or the controlled vocabulary specific to the databases for the condition specified.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Levels of Evidence

Level	Type of Evidence
1++	High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
1+	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g., case reports, case series
4	Expert opinion

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

These guidelines were compiled by a committee comprising a family physician, pharmacists, psychologists, psychiatrists and a patient representative appointed by the Ministry of Health. They were developed based on best available current evidence and expert opinion.

Rating Scheme for the Strength of the Recommendations

Grades of Recommendation

Grade	Recommendation
A	At least one meta-analysis, systematic review of randomised controlled trials (RCTs), or RCT rated as 1++ and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or

Grade	Recommendation
C	Extrapolated evidence from studies rated as 1++ or 1+ A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+
GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group

Cost Analysis

See Section 12 of the original guideline document for cost-effectiveness issues.

Method of Guideline Validation

Not stated

Description of Method of Guideline Validation

Not applicable

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis, evaluation, and management of bipolar disorder

Potential Harms

- Typical antipsychotics, such as haloperidol, are associated with extra-pyramidal side effects.
- Atypical antipsychotics, such as olanzapine, are associated with weight gain, hyperglycaemia and hypercholesterolemia. Olanzapine and risperidone have also been associated with increased morbidity and mortality risk in the elderly.
- It has been reported by the United States Food and Drug Administration (US FDA) that patients taking antiepileptic drugs have about twice the risk of suicidal thoughts and behaviours (0.43%) compared with patients receiving placebo (0.22%).
- Long-term use of benzodiazepines is discouraged due to possible adverse psychological and physical effects, including tolerance, physical dependence and withdrawal symptoms upon cessation of use.
- Side effects such as cognitive impairments as well as the stigma of undergoing electroconvulsive therapy (ECT) have to be taken into account.
- Lithium is associated with an increased risk of manic relapse on discontinuation after less than 2 years on treatment.

- Rapid cycling patients have worsened outcomes with selective serotonin reuptake inhibitors (SSRIs) or the other newer antidepressants.
- Antidepressant medication alone without a mood stabiliser carries larger risks of manic or hypomanic relapses. However, abrupt or rapid discontinuation of clinically effective antidepressant treatment was associated with a significantly shorter time to first new episode of major depression.
- Women on combined oral contraceptive pills who are concurrently taking carbamazepine and/or lamotrigine should be advised of the risk of decreased contraceptive effect as a result of drug interactions.
- Use of sodium valproate, lithium carbonate, lamotrigine and carbamazepine in pregnancy is associated with increased risk of foetal malformations and perinatal complications. In particular, children exposed to sodium valproate or polypharmacy in utero are more prone to poor long-term neurodevelopmental outcomes.
- First-trimester use of paroxetine is associated with odds ratios of 1.46 (95% confidence interval [CI] 1.17–1.82) for cardiac defects and 1.24 (95% CI 1.08–1.43) for aggregated congenital defects.
- SSRI use in late gestation may be associated with increased risk of persistent pulmonary hypertension of the newborn and neonatal behavioural syndrome.
- Antipsychotics, as an entirety, are associated with increased prolactin up to 10 times normal and amenorrhea in 17% to 78% of female users. Atypical antipsychotics, as a group, may be associated with increased risk of gestational metabolic complications and large gestational weight, as well as foetal malformations (especially with clozapine). On the other hand, typical antipsychotics, as a group, may be associated with limb defects, other foetal anomalies and perinatal complications, but appear to show less association with gestational metabolic complications.

Contraindications

Contraindications

Benzodiazepines should be avoided in pregnancy.

Qualifying Statements

Qualifying Statements

- These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.
- The contents of this publication are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case. These guidelines should neither be construed as including all proper methods of care, nor exclude other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient, in the light of the clinical data presented by the patient and the diagnostic and treatment options available.
- Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence may supersede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review 3 years after publication, or if new evidence appears that requires substantive changes to its recommendations.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Audit Criteria/Indicators

Quick Reference Guides/Physician Guides

Resources

Slide Presentation

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Singapore Ministry of Health. Bipolar disorder. Singapore: Singapore Ministry of Health; 2011 Nov. 68 p. [125 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011 Nov

Guideline Developer(s)

Singapore Ministry of Health - National Government Agency [Non-U.S.]

Source(s) of Funding

Singapore Ministry of Health

Guideline Committee

Bipolar Disorder Workgroup

Composition of Group That Authored the Guideline

Workgroup Members: Dr Mok Yee Ming (*Chairman*), Consultant/Deputy Chief, Department of General Psychiatry, Institute of Mental Health; Dr Chan Herng Nieng, Consultant, Department of Psychiatry, Singapore General Hospital; Mr Chee Kok Seng, Principal Clinical Pharmacist, Community Wellness Centre; Dr Chua Tze-Ern, Associate Consultant, Mental Wellness Service, KK Women's and Children's Hospital; Dr Lim Boon Leng, Consultant, Department of Psychological Medicine, Khoo Teck Puat Hospital; Ms Marziyana A Rahman, Principal Manager, Community Mental Health, Primary & Community Care, Ministry of Health; Dr Peh Lai Huat, Senior Consultant, Department of Psychological Medicine, Changi General Hospital; Pastor Song Cheng Hock, Patient representative; Dr Tung Yew Cheong, Senior Family Physician, Toa Payoh Polyclinic; Dr Patricia Yap, Senior Clinical Psychologist, Department of Psychology, Institute of Mental Health; Dr Michael Yong, Director of Psychological Medicine, Department of Medicine, Alexandra Hospital/Jurong Health Services

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the Singapore Ministry of Health Web site .

Print copies: Available from the Singapore Ministry of Health, College of Medicine Building, Mezzanine Floor 16 College Rd, Singapore 169854.

Availability of Companion Documents

The following are available:

- Bipolar disorder. Executive summary of recommendations. Singapore: Singapore Ministry of Health; 2011 May. 12 p. Electronic copies: Available in Portable Document Format (PDF) from the Singapore Ministry of Health Web site .
- Various slide sets and videos for pharmacological interventions for both acute treatment, maintenance, and substance misuse and reproductive health issues; psychological interventions; suicide prevention; and monitoring are available from the Singapore Ministry of Health Web site .

In addition, self-assessment questions and clinical quality improvement parameters are available in the original guideline document .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on March 14, 2013. This summary was updated by ECRI Institute on July 10, 2013 following the U.S. Food and Drug Administration advisory on Valproate. This summary was updated by ECRI Institute on December 18, 2014 following the U.S. Food and Drug Administration advisory on Ziprasidone. This summary was updated by ECRI Institute on May 24, 2016

following the U.S. Food and Drug Administration advisory on Olanzapine. This summary was updated by ECRI Institute on May 31, 2016 following the U.S. Food and Drug Administration advisory on Aripiprazole (Abilify, Abilify Maintena, Aristada).

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